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Review

Depression and anxiety in childhood epilepsy: A review

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ABSTRACT

Population based studies suggest that symptoms of depression and anxiety are more frequent in children and adolescents with epilepsy compared with the general population. In terms of the manifestations of symptoms of depression and anxiety, there would appear to some symptoms unique to epilepsy in that they are associated with seizures and/or antiepileptic medications but these idiosyncratic symptoms remain under reported and have not been extensively studied. In terms of correlates of significant symptoms of depression and anxiety in children with epilepsy, some reports indicate that seizure variables (e.g., seizure frequency) and use of polytherapy are associated with increases in symptoms whereas other studies have not found this relationship. Child and family attitude/adaptation to epilepsy may also be risk factors for depression and anxiety but more research is needed in this area. The assessment of symptoms of depression and anxiety in children with epilepsy can be challenging given the possible role of seizures and AEDs, and comprehensive assessment will involve the use of screening measures, diagnostic interviews and a consideration of epilepsy specific factors. There have been few studies carried out with respect to the treatment of symptoms and depression and anxiety in children and adolescents with epilepsy. There is a significant need for a greater understanding of the nature of symptoms of depression and anxiety in children with epilepsy to inform treatment decisions. While treatment of epilepsy specific symptoms of depression and anxiety may involve an evaluation of the current epilepsy treatment protocols, there may also be a need for pharmacological and/or psychotherapeutic interventions in the treatment of symptoms of depression and anxiety which are not epilepsy specific.

1. Introduction

Children with epilepsy have been reported to be at high risk for behavioural and psychiatric disorders in population based studies.[1,2] Elevated rates of depression, anxiety and suicidal attempts have been reported in adults with epilepsy[3–6] and it is increasingly being realised that both depression and anxiety in youth with epilepsy are common but often unrecognized disorders.[7,8] Therefore, the early identification and treatment of both conditions is crucial to minimize the risk for suicide and negative impact on quality of life. The reported frequency and severity of emotional and behavioural problems in children with epilepsy would suggest that a comprehensive epilepsy service should provide assessment and treatment of psychiatric problems[9] and there should be regular monitoring of psychological adjustment of children with epilepsy.[2] However, such difficulties are often either unrecognized or assessment and intervention are not available. Ott et al.[10] reported that although 60% of children with epilepsy in a clinic based study met criteria for one or more psychiatric diagnoses, nearly two-thirds of those with one or more diagnoses were not in receipt of treatment for the conditions.

The fourth edition (text revised) of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)[11] classifies mood disorders into depressive disorders including major depressive disorder (MDD), dysthymic disorder, and depressive disorder NOS (not otherwise specified), and bipolar disorders. In studies of children with epilepsy distinctions between different types of depressive disorders have not usually been made and bipolar disorders have not been widely studied. The essential feature of a major depressive episode is a period of at least two weeks in which there is either low mood or loss of interest/pleasure in most activities and in children and adolescents the mood may be irritable as opposed to sad.[11] Other possible symptoms include changes in appetite or weight, sleep and psychomotor activity, decreased energy, feelings of worthlessness or guilt, difficulty thinking, concentrating or making decisions or recurrent thoughts of death or suicidal ideation, plans or attempts.[11] The point prevalence of depression in children is 1–2%, increasing to 3–8% in

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adolescents and by the end of adolescence approximately 1 in 5 adolescents will have experienced at least one depressive episode.[12]

While the focus has often been on depression in individuals with epilepsy, symptoms of anxiety and anxiety disorders may be just as common and disabling.[13] The DSM-IV-TR classifies anxiety into several types, including panic disorder, obsessive-compulsive disorder (OCD), agoraphobia, social phobia, specific phobia, post-traumatic stress disorder (PTSD), and generalized anxiety disorder (GAD). Again distinctions between different types of anxiety disorder have not usually been made in studies of children with epilepsy. In the paediatric population, anxiety disorders affect 5–18% of children, 0.3–12.9% of preadolescents, and 0.6–7% of adolescents.[14] In individuals without epilepsy depressive and anxiety disorders tend to occur together with a high frequency, and anxiety is often co morbid with depression in epilepsy.[15,16] Therefore, for the purposes of this review article depression and anxiety are discussed together although where differences exist they will be discussed separately.

2. Methodology

In order to identify appropriate studies and reviews/position papers for inclusion a literature search was undertaken in March 2011 using the electronic databases PubMed and PsychINFO. The search was conducted using the using the following keywords in 'title': epilepsy + depression + children/adolescents, and epilepsy + anxiety + children/adolescents as illustrated in Fig. 1. The original search yielded 24 unique papers. To meet criteria for inclusion in this review a study or review position/paper had to: (1) be written in English, (2) report on the prevalence and/or risk factors for symptoms of depression/anxiety in children/adolescents (0–18 years) with epilepsy, (3) report on the treatment of depression/anxiety in children/adolescents with epilepsy, (4) review the literature or put forward a view/position on depression/anxiety in children/adolescents with epilepsy. The objectives of the review were to review papers focussing on the prevalence and correlates of depression and/or anxiety in childhood epilepsy and to examine issues with regard to manifestation of symptoms, assessment of such symptoms and intervention/treatment in this population.

Sixteen papers met inclusion criteria after the initial search. Of these 16, nine papers focussed primarily on the prevalence of and/or risks for depression/anxiety in children/adolescents with epilepsy, four were reviews/position papers on depression/anxiety in children/adolescents with epilepsy, two focussed on treatment of depression/anxiety in children/adolescents with epilepsy, and one paper focussed on academic achievement in children/adolescents with epilepsy and depression. Excluded papers included articles focussed on depression/anxiety in parents of children with epilepsy, siblings of children with epilepsy, and studies published in languages other than English.

None of the 16 studies included population based data on the prevalence of depression/anxiety in children/adolescents with epilepsy. In order to identify population based studies and further pertinent studies the following epilepsy/neurology journals were electronically searched using the terms 'depression' and 'anxiety': *Developmental Medicine and Child Neurology, Epilepsia, Epilepsy & Behavior, Epilepsy Research, Seizure*, and *Journal of Child Neurology*. Reference lists from already included articles and articles identified via the journal based search were also used to identify relevant papers. Six population based studies and one meta-analysis of

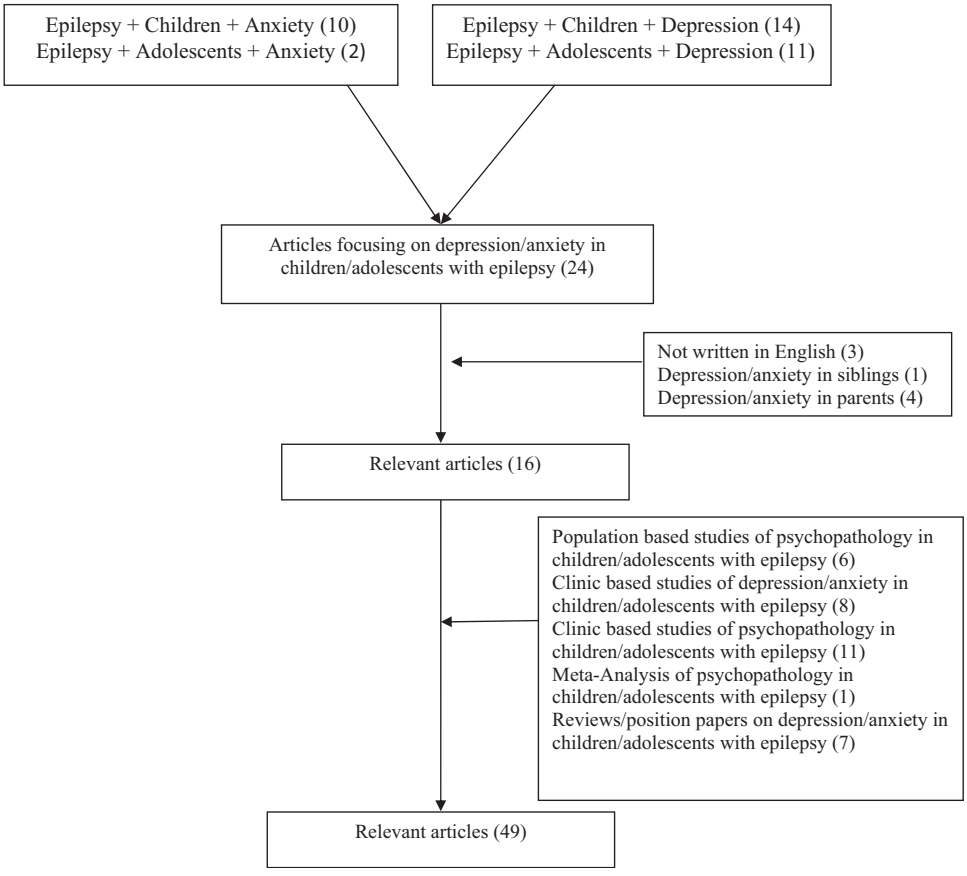

Fig. 1. Search process in identifying articles for the review.

psychopathology in children with epilepsy including measures of anxiety and/or depression were found and eight clinic based studies of children with epilepsy which included specific measures of depression and/or anxiety were identified. Eleven studies focussing on psychopathology in children with epilepsy which included measures of depression/anxiety were found. A further seven review/position papers focussing wholly or partially on depression/anxiety in children/adolescents with epilepsy were also identified via this secondary search. A total of 49 papers were identified for the purposes of the review. Studies involving measures of psychopathology in children with epilepsy which did not include specific measures of depression and/or anxiety were not reviewed.

3. Prevalence rates of depression and anxiety in children with epilepsy

Population based studies are important with regard to identifying prevalence rates of psychiatric disorders in children with epilepsy, as epilepsy is characterised by a spectrum of severity. Reported rates of psychopathology from specialised epilepsy clinics will be higher than rates from population samples as these clinics tend to treat children from the more severe or complex end of the epilepsy spectrum.[17] Two population based studies included children with intellectual disability and epilepsy and these studies are referred to in the section on childhood epilepsy and intellectual disability.[18,19] Table 1 illustrates the four identified population based studies that have focussed on psychopathology in children with epilepsy and included measures of either depression and/or anxiety.

The differences in reported prevalence rates of anxiety and depression in the population based studies are likely to be reflective of both the criteria used to identify/diagnose children with depression and/or anxiety and also how children with epilepsy were ascertained. In only two of the studies[2,20] were DSM-IV[21] criteria used to identify depression and/or anxiety. Davies et al.[2] used the term 'emotional disorder' as a proxy for depression and/or anxiety and did not report separate rates for both disorders while Hedderick and Buchhalter[20] used the term 'mood disorder' presumably to denote depressive disorders. Regarding the identification of epilepsy, in the Davies et al.[2] and McDermott et al.[22] studies parents were asked to indicate whether their child had epilepsy. In the Berg et al.[23] study which had the largest number of participants, the children/adolescents had been participating in the Connecticut Study of Epilepsy a longitudinal study of children recruited from the offices of paediatric neurologists in Connecticut. Hedderick and Buchhalter[20] used data from the Rochester Epidemiology project based on all incident cases of epilepsy diagnosed in the Rochester area over a 15-year period. Davies et al.[2] and McDermott et al.[22] were able to use comparison data from control children with other health conditions and control children from the general paediatric population, to show that the prevalence of difficulties with depression and/or anxiety were significantly higher in children with epilepsy compared with both types of controls. Davis et al.[2] reported that rates of 'emotional disorder' for children with 'complicated epilepsy' were similar to rates for those with 'uncomplicated epilepsy' suggesting that difficulties with anxiety and depression are not restricted to children with epilepsy who have additional neurological or intellectual difficulties. 'Complicated epilepsy' included children with severe learning difficulties (vocabulary quotient <60), speech or language difficulties, cerebral palsy, other physical impairments, and congenital conditions.[2]

Studies of prevalence rates of depression and/or anxiety for children with epilepsy drawn from clinic based samples have reported rates of depression and/or anxiety with respect to norms on standardised behavioural checklists and/or comparisons with mean scores of children acting as controls. In the majority of clinic based studies children with epilepsy who are functioning in the intellectually disabled range have been excluded. In a meta-analysis of studies of psychopathology in children with epilepsy Rodenburg et al.[26] reported that children with epilepsy were more likely to have difficulties with 'anxious/depressed' domains on checklists (mainly the CBCL)[27] compared with normative controls via parent report, teacher report and self-report. Children with epilepsy were also likely to have difficulties with 'anxious/depressed' domains compared with healthy study controls on parent report, and children with another chronic illness on parent but not teacher report. However, compared with siblings, children with epilepsy were not reported to have a greater incidence of difficulties on depression/anxiety domains, suggesting family factors may play a role in the elevated levels of symptoms of depression and anxiety in children with epilepsy.

Table 1
Population-based studies of depression/anxiety in children with epilepsy.

References	Location	Sample source	Age of sample	Sample size	Measures	Prevalence of depression/anxiety
Berg et al.[23]	USA	Connecticut Study of Epilepsy	5.9+9 years[a]	501	Review of medical records and interview about presence of conditions	67 (13.4%) of children with epilepsy met criteria for 'Depression', 6 (1%) met criteria for 'Bipolar Disorder', 25 (5%) met criteria for 'Anxiety'.
Davies et al.[2]	UK	British child and adolescent mental health survey	5–15 years	67	DAWBA and DSM-IV criteria	7 (16.7%) with 'uncomplicated' epilepsy and 4 (16%) of those with 'complicated' epilepsy met criteria for an 'Emotional Disorder' compared with 6.4% of those with diabetes and 4.2% of the general paediatric population.
Hedderick and Buchhalter[20]	USA	Rochester epidemiology project	<16 years of age	134	Review of medical records with respect to DSM-IV criteria	16 (12%) of children with epilepsy had a DSM-IV 'Mood Disorder'.
McDermott et al.[22]	USA	Data from national health interview survey	5–17 years	111	BPI	29 (24%) of children with epilepsy had significant 'Anxiety' compared with 16.5% of children with cardiac difficulties and 7.5% of general paediatric population

DAWBA, Development and Well-Being Assessment[24]; BPI, Behaviour Problem Index[25]; DSM-IV, diagnostic and statistical manual of mental disorders fourth edition.[21]
[a] Children originally diagnosed at an average age of 5.9 years and followed up 9 years later.

A number of clinic based studies have employed depression specific or anxiety specific instruments and/or diagnostic interviews. Studies that have employed the Childhood Depression Inventory[28] have reported that between 12 and 32% of children with epilepsy score in the at-risk range[29–36] although the cut-offs used to determine at-risk status have not always been the same in clinic based studies. The highest reported rate by Tosun et al.[31] was for a group of adolescents with epilepsy who were selected as they had low academic performance. With regard to other depression specific instruments Roeder et al.[37] reported that 36% of children screened positive for symptoms of depression on the Short Mood and Feelings Questionnaire (SMFQ).[38] Turky et al.[39] used the Moods and Feelings Questionnaire (MFQ)[40] and reported that although 39.6% screened positive for depression on the MFQ based on parent report, only 23.1% met criteria based on adolescent self-report. Dunn et al.[9] reported that only 9.6% of children and adolescents met criteria for either dysthymia or major depression on the Child Symptom Inventory (CSI)[41] or Adolescent Symptom Inventory.[42] Rates of depression in children with epilepsy employing DSM-IV diagnostic interviews in clinic based samples have ranged from 12%[7] to 36.5%.[43] The highest rate of depression reported by Thome-Souza et al.[43] was for a clinic based study in which the median IQ was 80 and 10 children had an IQ score below 55.

With regard to suicidal ideation Caplan et al.[7] reported that 20% of children with epilepsy had a rate of suicidal ideation in a clinic based sample which was significantly more than controls (9%) and the 5.2% rate in the general population.[44] Oğuz et al.[34] reported that suicidal ideation was noted in 17.1% of children with epilepsy and none of the control participants in a clinic based sample. It has been suggested that bipolar disorders are rarely diagnosed in the paediatric epilepsy population.[45] Berg et al.[23] reported that only 1% of a population based sample of children with epilepsy had bipolar disorder. Dunn et al.[9] reported that 5.4% of 74 adolescents from a clinic based sample screened in the at-risk range for bipolar disorder on the ASI compared to only 0.9% of those in the standardisation sample. However, no data for the prevalence of bipolar disorder based on a diagnostic interview was reported on in this study.

Compared with depression, anxiety disorders have not been as frequently the focus of clinic based studies of children with epilepsy. The instrument most commonly used in studies has been the Revised Children's Manifest Anxiety Scale (RCMAS).[46] Loney et al.[30] reported that only one child of 22 children presenting with a first seizure exhibited a clinically significant total anxiety score (>2SD from the mean) on the RCMAS. However, eight of 22 children displayed 'significant' symptoms of anxiety (>1SD from the mean) in this study. Williams et al.[47] reported that 23% of children with epilepsy had scores higher than 1SD above the mean and 5% had scores 2SD above the mean on the RCMAS. Using the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS)[48] diagnostic interview Jones et al.[49] reported that 35.8% of children experienced an anxiety disorder. Caplan et al.[7] reported a similar rate using the same instrument. The highest reported rate of anxiety disorder in children with epilepsy (48.5%) was reported in a study in Jordan by Alwash et al.[50] who employed DSM-IV criteria but did not employ standardised screening or diagnostic measures. Adewuya and Ola[51] reported a rate of 31.4% in a Nigerian study using the Diagnostic Interview for Children Version IV (DISC-IV).[52]

On screening instruments and diagnostic interviews children with epilepsy have scored significantly higher than controls[7,30,49,50] or had similar levels of anxiety to controls.[32] Studies of anxiety symptoms have not focussed on types of anxiety disorder in epilepsy with the exception of Dunn et al.[9] In this study using the ASI/CSI, 1.8% of children with epilepsy met cut-off for generalized anxiety disorder, 34.9% for specific phobia, 34.9% for obsessions, 8.9% for compulsions, 33.7% for postramatic stress disorder, 1.9% for social phobia, and 6.0% for separation anxiety disorder. In the 13–14-year-old group in this study 36.5% met criteria for panic disorder. However, when the screening instrument was followed by a diagnostic interview only 3% of those who screened positive met criteria for PTSD, 50% who screened positive met criteria for specific phobia, none met criteria for panic disorder, 63% of screen positives met criteria for social/specific phobia and 83% met criteria for obsessive–compulsive disorder. This suggests that the screening instrument used in this study was producing a significant number of false positives and emphasises the need for screening/surveillance to be followed up by diagnostic interviews in studies reporting the prevalence of anxiety in children with epilepsy.

4. Manifestation of depression and anxiety in epilepsy

An issue with regard to the reported rates of anxiety and depressive symptoms in children with epilepsy concerns whether symptoms of depression and anxiety are similar in children with epilepsy to symptoms in children without epilepsy. In the case of depression, Plioplys[8] suggests that to date there is no research data demonstrating that depression in young people with epilepsy is characterised by a different phenomenology, clinical course or treatment compared with depression in young people without epilepsy. However, in a consensus statement on depression in epilepsy Barry et al.[53] emphasise that it is important to recognize that although symptoms of depression and anxiety may be common in children and adolescents with epilepsy, they may not present with the 'classic' symptoms of these disorders. Symptoms of depression associated with epilepsy may be temporally related to the occurrence of seizures, either before a seizure (preictally), as a clinical expression of the seizure (ictal), following a seizure (postictally) or between seizures (interictal). These symptoms are the least studied in a systematic manner and are not often investigated by clinicians in evaluations of individuals with epilepsy.[53] According to Barry et al.[53] these symptoms would not be detected with the standard diagnostic instruments and studies identifying the prevalence of depression in epilepsy have not discriminated between an ictal, interictal, preictal, or postictal occurrence. In a similar vein for symptoms of anxiety, it has been suggested that it is useful to distinguish between epilepsy-related preictal, ictal, postictal, and interictal anxiety symptoms and "comorbid anxiety" which is unrelated to epilepsy.[13] Again anxiety symptoms of this nature remain under researched in children and adolescents with epilepsy and none of the population based studies or clinic based studies identified in this review examined symptoms of depression or anxiety that are temporally related to the occurrence of seizures. Another consideration with regard to symptoms of depression and anxiety in children with epilepsy concerns the effects of anti-epileptic drug (AED) treatments. Most AEDs can cause symptoms of depression in young people with epilepsy.[54] If an AED with mood stabilising properties is discontinued symptoms of a mood disorder which was in remission due to effects of AED can return.[54] The side effects of AEDs might also include anxiety.[55]

5. The bidirectional nature of epilepsy and depression and anxiety?

In children with epilepsy the relationship between seizures and symptoms of depression and anxiety has increasingly been addressed with regard to possible shared underlying mechanisms. Kanner[56] hypothesises that there is a bidirectional relationship between mood disorders and epilepsy with seizures acting as a risk

factor for the onset of depression, and depression acting as a risk factor for the onset of epilepsy which may be explained by the pathogenic mechanisms operant in both disorders. While people with epilepsy are at greater risk of developing depressive disorders there is also emerging evidence that individuals with depression are at higher risk than the normal population of developing epilepsy.[57,58] With regard to onset of symptoms of anxiety/depression, and onset of epilepsy Loney et al.[30] reported that children with a first seizure had significantly higher anxiety scores compared with normative scores, and children with a first seizure also had significantly higher scores than controls compared with normative scores on a measure of depression. In a study by Jones et al.[49] 24 (45.3%) children with epilepsy met diagnostic criteria for a DSM-IV disorder before the diagnosis of epilepsy and first recognized seizures. Of these 24, eight had diagnosis of an anxiety disorder and five met criteria for a depressive disorder. Hesdorffer et al.[58] reported that children and adults with incident unprovoked seizure were 1.7 times more likely to have a history of major depression before seizure onset. However, Austin et al.[59] reported that children with new onset epilepsy had significantly higher scores than sibling controls on some scales of the CBCL[27] but not the anxious/depressed scale, although the difference in scores on the anxious/depressed scale approached significance for a group of children with previous seizures in this study. Therefore, it would appear that a number of children who develop epilepsy have significant symptoms of depression and anxiety before seizure onset although for other children with epilepsy, symptoms of depression and/or anxiety develop after the onset of seizures. A complicating factor in the temporal relationship between seizures and symptoms of anxiety and depression concerns whether or not seizures have been occurring before they are first reported. It is possible that seizures could be occurring during sleep, or during waking without being identified as seizures but presenting as non-compliance or low mood. It is also possible that abnormal EEG activity without seizures has been occurring well before a first reported seizure. There is also the possibility that there is a primary brain disorder of brain development that is causing both epilepsy and depression.

6. Correlates of depression and anxiety in children and adolescents with epilepsy

Correlates of depression and anxiety in childhood epilepsy have been examined with respect to epilepsy/seizure correlates, AEDs, child demographics, and child/family adaptation to epilepsy.

In terms of epilepsy/seizure correlates, variables that have been focussed on include seizure type/epilepsy syndrome, seizure frequency/severity, and age of seizure onset. Seizure type has not been related to symptoms of anxiety or depression in most studies.[29,34,36,37,47] However, it has been reported that the presence of seizure foci in the temporal lobe may represent a higher risk for the development of depression and anxiety.[43] Caplan et al.[7] reported that there was a significantly higher rate of depression and combined depression and anxiety disorder in a group of children with Complex Partial Seizures (CPS) compared with a group of children with Childhood Absence Epilepsy (CAE), but a higher rate of anxiety disorders in the CAE group. With regard to seizure frequency/severity, Oğuz et al.[34] reported that increased seizure frequency was associated with increases in anxiety and depression scores and Turky et al.[39] reported that poor seizure control predicted higher depression scores. Adewuya and Ola[51] reported than increased symptoms of anxiety were associated with an increased frequency of seizures. Alwash et al.[50] also reported that symptoms of anxiety were higher when seizures were less well controlled. However, Dunn et al.[35] did not find seizure severity a significant predictor of depressive symptoms and Cusher-Weinstein et al.[29] did not find that frequency or severity predicted scores on the CDI. Ettinger et al.[36] did not find that the number of recent seizures was correlated with scores on depression or anxiety measures. Age of seizure onset has not been found to be a significant predictor of anxiety or depression in most studies of children with epilepsy.[34–37] However, Cusher-Weinstein et al.[29] reported that scores on the interpersonal domain of the CDI were significantly correlated with younger age of onset. Increased duration of epilepsy has not been associated with symptoms of anxiety or depression[36,37] although Cusher-Weinstein et al.[29] reported that scores on the interpersonal domain of the CDI were significantly correlated with longer duration of epilepsy.

In a review Ekinci et al.[60] suggested that in most of the studies of adolescents with epilepsy, AED use or type of AED have not been found to be consistent predictors of depression. However, there have been associations reported between some drugs and symptoms of depression and anxiety in some young people with epilepsy and also reported increases in such symptoms for children or adolescents on more than one AED. Brent et al.[61] reported an association between phenobarbital and depression in children with epilepsy although it was only reported in children with a family history of depression. Anxiety and 'nervousness' have been reported to be associated with drugs such as felbamate and topirimate and with withdrawal of AEDs.[62] Roeder et al.[37] and Adewuya and Ola[51] reported that a greater number of AEDs was the only variable that was independently predictive of more severe symptoms of depression. Williams et al.[47] noted that children with epilepsy who were on polytherapy as opposed to monotherapy were more likely to experience significant anxiety symptoms. Oğuz et al.[34] found that children with epilepsy who were receiving more than one epileptic drug had higher anxiety and depression scores compared to those were taking just one drug and Cusher-Weinstein et al.[29] reported that polytherapy was associated with higher scores on the CDI. However, one study by Ettinger et al.[36] reported that neither scores on a measure of depression or a measure of anxiety differed based on whether the child was on monotherapy or polytherapy.

In relation to child demographics, child age and gender have been the two variables most frequently focussed on. Twice as many female adults are depressed as male adults and this difference tends to develop in early adolescence[63] with girls having twice the risk of developing depression than boys after puberty.[64] Female gender has been associated with higher mean depression scores in some studies of children with epilepsy.[39,65] However, gender differences in studies of depressive symptoms have not been noted in most studies of children with epilepsy.[32,35,36,38] A study by Buelow et al.[33] suggests that level of IQ may play a role in symptoms of depression in girls with epilepsy. This study found while males tended to have more stable values across the IQ groups, females displayed more variability. While 8% of females with high IQ (101–130) in the study were deemed at risk on the CDI the figure was 43% for those with low IQ (56–84). Despite the well-known female predominance of anxiety in the general population the predominance has not been widely reported in children with epilepsy[60] and a number of studies have not found a significant effect of gender on anxiety symptoms in children with epilepsy.[31,36,47] However, McDermott et al.[22] did report that male gender was protective against having 'anxiety'.

Symptoms of depression in younger children are less likely to be present than symptoms in adolescents and studies which employ measures of depression may exclude younger children who would not be able to complete self-report measures of symptoms. Thome-Souza et al.[43] reported that the diagnosis of depression was higher in a clinic referred group of children with epilepsy who were aged 13–17 years compared with 7–12-year

olds. Oğuz et al.[34] reported that the percentage of significant depression scores was 13.3% in a 9–11-year-old group and 40% in a 12–18-year-old group. However, some studies have not found age to be a significant predictor of depressive symptoms.[26,34,35] It has been suggested that older children with epilepsy are at risk for higher levels of anxiety than younger children[66] and significant differences in mean anxiety scores compared with controls were more likely in an older group of children compared with a younger cohort of children in a study by Oğuz et al.[30] However, increasing age was not associated with an increase in the diagnosis of anxiety disorders in the study of Adewuya and Ola.[51]

With regard to correlates of psychopathology in children with epilepsy there has been an increasing emphasis on the possible role of child and family adaptation to a diagnosis of epilepsy. Epilepsy in adolescence is associated with significant stigma[67] and Meador[68] asserts that the perception patients have of their condition affects their quality of life more than the condition itself. Although there has been limited research on child attitudes towards epilepsy and stigma it is likely that having epilepsy is perceived by many as stressful. Dunn et al.[35] reported that there was an influence of child attitude towards having seizures and satisfaction with family relationships on scores on a measure of depression. In this study youths with epilepsy who had a negative attitude towards having seizures and had a negative evaluation of family relationships had significantly higher rates of depressive symptoms. Rodenburg et al.[69] suggest that family related factors, particularly quality of child parent relationship, and specifically parental rejection are pivotal in psychopathology of children with epilepsy. It is clear that having a child who develops epilepsy can disrupt family functioning although it is not yet clear how responses to the diagnosis of epilepsy among the affected child and their parents impacts on symptoms of depression and anxiety in affected children. With regard to parental depression, having a child with epilepsy appears to be a risk factor for symptoms of parental depression. Ferro and Speechley[70] reviewed the literature on depressive symptoms among mothers of children with epilepsy and concluded that a relatively high proportion of mothers of children with epilepsy display depressive symptoms, and that available evidence suggest that a negative relationship exists between such symptoms and child health outcomes. Cusher-Weinstein et al.[29] reported that parents of children with elevated scores on the CDI reported significantly higher scores in the parental distress domain of the Parenting Stress Index. Adewuya and Ola[51] reported than higher child anxiety scores were associated with higher scores on measures of family stressors, perception of epilepsy stigma, parental psychopathology and family stressors.

7. Symptoms of depression and anxiety in children with epilepsy and intellectual disability

Approximately one quarter of children with epilepsy are functioning in the intellectually disabled (ID) range (IQ < 70).[71] The presence of intellectual disability in children is associated with increased levels of psychopathology[72] although psychiatric disorders in children with intellectual disability may be under recognized and under treated. The concept of 'diagnostic overshadowing',[73–75] a phenomenon which highlights that clinicians may emphasise a client's intellectual disability and under emphasise psychopathology[76] has been proposed for this lack of identification and treatment. The assumption is that intervention is not needed because the abnormal or atypical behaviour is an inherent part of intellectual disability and may lead to disorders being missed and untreated.[77] However, there are difficulties in diagnosing some disorders in an ID population and the criteria that have been developed for people without intellectual disability may not be as valid in children with ID.[78] It is not clear if epilepsy and intellectual disability combine to increase the risk of psychopathology over and above that due to intellectual disability alone.

Steffenburg et al.[18] reported on a population based study of children with epilepsy and intellectual disability. Of the 90 children who were examined only 3% had 'overanxious disorder' as a main diagnosis and no rate was reported for mood disorders. It must be noted that approximately one third of the children could not be classified with respect to psychiatric disorder due to having profound intellectual disability and no controls with intellectual disability without epilepsy were used in the study. Using population based data Lewis et al.[19] did not find that young people with epilepsy and ID and young people with ID without epilepsy differed significantly with regard to the prevalence of anxiety symptoms on the anxiety subscale of the Developmental Behaviour Checklist.[79] Assessing depressive symptoms in children with epilepsy and intellectual disability may present significant assessment difficulties as on measures such as the CDI many children with ID would struggle to read and as a result respond to items.

8. Assessment and diagnosis of depression and anxiety in children with epilepsy

Although published population based studies suggest that a significant minority of children with epilepsy are at risk for clinically significant symptoms of anxiety and depression the identification of such symptoms is not without challenges. The clinical presentation of these symptoms in individuals with epilepsy can create additional assessment challenges for clinicians.[80] With regard to informants it is vital that where possible children and adolescents are asked about symptoms, as given the internalizing nature of symptoms of depression and anxiety informants such as parents and teachers may not be aware of depressive and anxiety symptoms the children are experiencing.[7,53] In paediatric patients in general, anxiety is usually more difficult to recognize than disorders with more overt clinical symptoms and unless a child presents with symptoms of school refusal, panic attack, or obsessive-compulsive symptoms, diagnosis is often delayed or missed.[62] For children with significant cognitive deficits there may be difficulties with regard to the ability to verbalise thoughts and feelings thus making identification of significant symptoms more problematic. In such cases parents and other potential informants should be asked about significant recent changes in behaviour, sleep patterns, activity levels, emotions, and patterns of social interaction. Taking a family history of psychiatric disorders will also be important for all children with epilepsy. A family history of depression was found to be a significant predictor of depression in children with epilepsy in a clinic based sample[43] and parental psychopathology was a correlate of child symptoms in a another study.[51] However, Caplan et al.[7] did not find that family history was a significant predictor of affective or anxiety disorders.

The differential diagnosis of depression and anxiety in children with epilepsy should include consideration of the effects of both seizures and of AEDs.[66] The occurrence of seizures can make it difficult to identify and isolate symptoms of anxiety. The fear of seizures or seizure-related accidents may lead to symptoms similar to agoraphobia and fear of having a seizure can be associated with separation anxiety about being away from parents or the home for children.[60] The differential diagnosis of seizures and panic disorder can also be difficult,[13] and panic attacks may mimic complex partial seizures.[66] Fear of embarrassment about having a seizure in public may also lead to symptoms similar to social phobia and result in withdrawal of the child from social activities and interactions.[13] It is important that a detailed history

of the context and development of the symptoms of anxiety and depression over time is garnered. Screening measures are designed to over identify those at risk for a disorder and produce more false positives than false negatives, and the use of anxiety specific and depression specific checklists will need to be supplemented by diagnostic interviews and comprehensive evaluation of symptoms taking into account possible effects of seizures and AEDs.

9. Treatment of depression and anxiety in children with epilepsy

The combination of cognitive behavioural therapy (CBT) and medication has been found to be superior to medication alone for the achievement of remission for paediatric depression,[81,82] and combination treatment appears to result in a more efficacious response than monotherapy in most, but not all studies.[82,83] The National Institute of Health and Clinical Excellence (NICE) guideline for the treatment of depression in young people[84] in the UK, emphasises the importance of psychological therapies for 'mild' depression and psychological therapies in addition to antidepressant medication for more 'severe' depression in young people aged 12–18. Psychological therapies include group and individual cognitive behavioural therapy (CBT), interpersonal therapy and family therapy. The use of antidepressant medication in those aged 12 or under should only be considered in very rare circumstances according to the NICE guideline. It must be noted that there are no references to epilepsy in the NICE guidelines. The consensus statement on evaluation and treatment of people with epilepsy and affective disorders[53] emphasises that the treatment of anxiety and depressive disorders in children requires the expertise of mental health professionals, including a child psychiatrist for psychopharmacological intervention, and a child psychiatrist, psychologist, psychotherapist, or social worker for the non-pharmacological treatments. Ekinci et al.[60] suggest that the treatment of depression in children with epilepsy should involve pharmacotherapy accompanied by cognitive-behavioural approaches as in the treatment of depression in children without epilepsy. However, the evidence base for pharmacological or non-pharmacological interventions in children with epilepsy is sparse. There have been no double-blind studies on the psychopharmacological treatment of mood and anxiety disorders in youth with epilepsy[53] and children with epilepsy tend to be excluded from the majority of drug studies.[8] Regarding non-pharmacological interventions for symptoms of anxiety and depression in children with epilepsy there has only been one published study of treatment involving psychotherapy to prevent development of depression in adolescents with epilepsy.[85]

Selective serotonin reuptake inhibitors (SSRIs) should be the first-line drugs in the treatment of depression and anxiety in children with epilepsy[8,53] due to their favourable side-effect profile, once a day administration, limited risk of fatal overdose, and safe drug–drug interactions with AEDs.[8] Tricyclic antidepressants are not recommended for use in children with epilepsy because of the potential increased seizure risk.[53] Prior to initiating psychopharmacological treatment for mood disorders in children with epilepsy it is important to obtain a detailed history to determine if the child's mood symptoms reflect AED withdrawal, high doses of AED polytherapy or use of AEDs with known behavioural side effects.[50] In the only study to report on the use of SSRIs in children/adolescents with epilepsy Thome-Souza et al.[86] reported on 36 children/adolescents with epilepsy diagnosed with depression based on DSM-IV criteria. In 29 children/adolescents sertraline was used and in the remaining seven children fluoxetine was prescribed. The authors reported that 35 of the 36 patients responded positively in that there was total or partial remission of depressive symptoms in the 12 months after introduction of the SSRI. Seizures were reported to have worsened in only two individuals in the 3-month period after the SSRI was introduced. All the children/adolescents in the study were functioning in the non-intellectually disabled range, and none had other chronic neurological disorders, metabolic or degenerative disorders or had experienced psychogenic non-epileptic events.

Interventions for young people with epilepsy and depression or anxiety may also involve psychotherapy. In the only published study on psychotherapy for children with epilepsy Martinović et al.[85] reported on 30 adolescents (aged 13–19) with epilepsy who met criteria for being at-risk for depression based on scores on a diagnostic interview and checklists. The adolescents were randomly assigned to short cognitive-behavioural interventions (CBI) or treatment as usual (TAU). CBI consisted of an individual treatment plan focussing on cognitive errors such as catastrophising, overgeneralization, personalisation, and selective abstraction. CBI was administered once a week for eight weeks and then one session per month over the next 4 months. TAU involved a similar number of sessions and therapeutic counselling without CBI. Seven to nine months after baselines three participants in the TAU group and none of the CBI group participants had their first depressive episode (this difference was not statistically significant). Follow up also revealed that scores on checklists were significantly lower in the CBI compared with TAU group. The CBI group also had significantly higher quality of life scores at follow-up.

There has been no research on family therapy interventions for children with epilepsy, although it has been recommended family involvement should be a key treatment component for children with mood disorders[53] given the posited impact of epilepsy on family functioning and hypothesised contributions of disruptions in family functioning to child psychopathology. Supportive individual or family therapy should address negative feelings towards epilepsy in light of the high level of stigma associated with the condition. Young people with active epilepsy are at significant risk for cognitive impairments,[71] attention deficit hyperactivity disorder (ADHD),[23] and autism spectrum disorder (ASD).[87] These may contribute directly or indirectly to depressive and anxiety disorders and in terms of management it is important that cognitive and behavioural impairments are identified and managed through appropriate educational provision and psychological and pharmacological interventions where necessary.

While there is now a well established link between epilepsy in young people and depressive and anxiety disorders there are still significant barriers with regard to treatment. Roeder et al.[37] reported that despite identification of significant depressive symptoms nearly two-thirds of parents of children with epilepsy did not seek help for their child's difficulties despite being advised to do so. They suggested that mental-help seeking behaviours among this group may differ from those found in the general population and it may be that parents do not consider such symptoms to be a prime focus being more concerned about seizure control. Another barrier to intervention may be that because problems such as hyperactivity, aggression, and impulsivity in children with epilepsy are more noticeable and observable such difficulties are more likely to lead to a psychological referral in comparison with the less obvious symptoms of depression and anxiety. It would appear to be essential that advice to parents and teachers of children with epilepsy should always include reference to the risks for the development of depression and anxiety disorders as well as reference to the common symptoms of such disorders.

10. Conclusion

The literature on depression and anxiety in children and adolescents with epilepsy was reviewed and available evidence suggests that 12–14% of those with childhood epilepsy have

depression based on population based data. There is less population based evidence in relation to prevalence rates of anxiety. There have been significant variations in instruments used to identify anxiety and depression and methods used to identify those with epilepsy in published studies. For both anxiety and depression the prevalence rates appear to be greater in young people with epilepsy than in the normal paediatric population and in children with other chronic medical conditions. The reason for the increased rates remains unclear. There is a suggestion that polytherapy may be associated with increased symptoms but no clear risk factors emerge from an examination of seizures. In relation to level of cognitive functioning it is not clear if subaverage cognitive functioning or intellectual disability increases the risk for the development of depression or anxiety.

The assessment and diagnosis of depression and anxiety in children with epilepsy may not be straightforward with a consideration of epilepsy variables and effects of AEDs being necessary in any diagnostic formulation. There is a potential for diagnostic confusion between panic attacks and complex partial seizures. Treatment of depression and anxiety with psychological therapies including CBT, and pharmacotherapy in children with epilepsy have tended to follow similar lines to those of children who do not have epilepsy and evidence about effective treatment in childhood epilepsy is sparse. The value of delineation of the cognitive and behavioural aspects of the phenotype and subsequent provision of appropriate educational social support have not been examined as preventative measures of symptoms of depression and anxiety in childhood epilepsy. On current evidence there would appear to be a strong case for epilepsy services to screen for depression and anxiety as part of a comprehensive assessment of possible learning and behavioural/psychiatric co morbidities. There is also a need for medical professionals working in such settings to receive training on issues involved in assessment, diagnosis and management and a need for research into the efficacy of such training with regard to the impact on ameliorating symptoms of depression and anxiety and improving quality of life in young people with epilepsy.

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